DRAFT NOTES FROM COCHRANE WORKING GROUP [WG] MEETING 10.7.15

PARTICIPANTS

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NOTES

At this second meeting of the WG, our goal was to develop a clear path towards producing a guidance document on methods for the systematic review of nonhuman toxicology studies for the purpose of generating evidence for use in public health policy and other fora. Our intention is to respond to the increasing adoption of "systematic reviews" by regulatory agencies and international institutions mandated to evaluate hazards of environmental and occupational exposures, including chemicals, mixtures, and food additives.

The WG reviewed a draft concept paper prepared by Mandrioli and Silbergeld, with critical inputs from several colleagues with experience and expertise in systematic reviews conducted in accordance with Cochrane Collaboration methods and policies. Concerns were raised about the need for awareness of the potential adverse impact on preventive health policies from any perception that decisions already in place cannot be relied upon, and also about setting the criteria so stringently [e.g., external validity of animal models] that the work of chemicals control will be hindered.

The WG generally supported the content and issues of concern identified in this draft with these additional considerations. The WG strongly emphasized the importance of including evidence from human studies (drawn largely from observational epidemiology and other sources) as a necessary part of the overall evidence relevant to evaluating hazards. The inclusion of human studies may require us to change the name of our work group, as suggested. In addition, the importance of including methods for systematic review of mechanistic studies was recognized, because of the reliance placed on these types of studies by regulatory agencies and international organizations.

Several additional topics and amendments were suggested by the WG, including: separating carcinogen and non carcinogen evaluations, consideration on mechanisms indirectness, challenges on performing "horizon scans" search, collaboration with National Library of Medicine for developing and validating PECOS statements and search terms, modular and scalable designs of systematic reviews (for example, the model should be applicable with one or more of the three streams of evidence – human, animal, in vitro), obstacles to obtaining data from toxicology due to lack of transparency and limited access to certain types of proprietary toxicological data (such as pesticide testing). These problems are similar to those that impeded systematic reviews of preclinical testing of drugs and proprietary practices in some clinical trials. A revised statement considering the above-mentioned observation will be drafted and circulated.

In the last part of our meeting, we discussed paths forward for this work. We debated the importance of a formal connection with the Cochrane Collaboration, and how such a connection should most appropriately be constructed in accord with the Policy Group guidelines.

On the "pro" side of a formal connection, there is a need for a "gold standard" for systematic reviews as the policy landscape at present is being occupied by a range of players, including the NIH, universities, consulting groups, and industry trade groups. For open regulatory processes, such as the US EPA, it is practically impossible to exclude any of these "vendors" or any reviews claiming to be systematic. In addition, a connection with Cochrane may encourage international adoption of a "gold standard" set of methods for the systematic review of toxicology, which would greatly reduce the resources of time and expertise needed to conduct such reviews.

On the "con" side, the process of developing this path and obtaining the appropriate recognition as part of Cochrane will be complex and not short. Moreover, several groups have already produced impressive handbooks – notably the National Toxicology Program and the USCF Navigation Guide – which may fulfil many of the needs identified by this WG. However, this will not provide users with the "protection" they need to reject insufficient or inaccurate methods proffered by entities with conflicts of interest.

The WG leaders pro tem propose to continue discussions with CC leaders, particularly those involved in other animal-related reviews as well as those knowledgeable about the policy steps involved, in order to develop a proposed path forward at the upcoming Exploratory Meeting to be held in Washington DC on May 4th, 2016, a first necessary step for moving forward the process according to the Cochrane Collaboration. This does not imply that this is the only way forward, and the results of this deliberation will be communicated and discussed with all attendees at the WG.